44. (Amended) The composition of claim 43, which comprises a peptide containing a sequence selected from the group consisting of: WRQTRKD (SEQ ID NO: 1); HYAKNPI (SEQ ID NO: 2); ATINKSL (SEQ ID NO: 3); RRRGMAI (SEQ ID NO: 4); THRLPSR (SEQ ID NO: 5); TKHGPRK (SEQ ID NO: 6); SLKRLPK (SEQ ID NO: 7); RLRGRNQ (SEQ ID NO: 8); WPFHHHR (SEQ ID NO: 9); HLYHHKT (SEQ ID NO: 10); THIHHPS (SEQ ID NO: 11); and MMMMMRL (SEQ ID NO: 12).

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45. (Amended) The composition of claim 44, which comprises a peptide containing a sequence selected from the group consisting of: THRLPSR (SEQ ID NO: 5); SLKRLPK (SEQ ID NO: 7); THIHHPS (SEQ ID NO: 11); and MMMMMRL (SEQ ID NO: 12).

46. (Amended) The composition of claim 45, which comprises a peptide containing the sequence SLKRLPK (SEQ ID NO: 7).

REMARKS

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Early consideration and allowance of the application are earnestly solicited.

Respectfully submitted,

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MARKED UP VERSION ATTACHED TO AMENDMENT IN SERIAL NO. 09/901,187

Marked up version of the paragraph starting at page 12, lines 22-30, thru page 13, lines 1-9, is below:

Such peptides can be found, for instance, by using phage display to select for those phage expressing a peptide on their surface that binds to α-synuclein, and determining what the peptide is. The inhibitory effect of that peptide, or any peptide for that matter, can also be tested to determine its usefulness as an agent for treating a Lewy body disease or synucleinopathy by using assays such as those disclosed herein or as disclosed in US Patent No. 6,184,351, which is incorporated herein by reference. Such peptides have been selected for their ability to bind to the C-terminal (approx. amino acids 113- 140), and the NAC portion (approx. amino acids 61 - 87) of α-synuclein, because this region is thought to be involved with the aggregation process. Several peptides that bind to the C-terminal portion are as follows (all peptides are given in 5′ to 3′ order): (1) WRQTRKD **(SEQ ID NO: 1)**; (2) HYAKNPI **(SEQ ID NO: 2)**; (3) ATINKSL **(SEQ ID NO: 3)**; (4) RRRGMAI **(SEQ ID NO: 4)**; (5) THRLPSR **(SEQ ID NO: 5)**; and (6) TKHGPRK **(SEQ ID NO: 6)**. Several peptides that bind to the NAC portion are: (1) SLKRLPK **(SEQ ID NO: 7)**; (2) RLRGRNQ **(SEQ ID NO: 8)**; (3) WPFHHHR **(SEQ ID NO: 9)**; (4) HLYHHKT **(SEQ ID NO: 10)**; (5) THIHHPS **(SEQ ID NO: 11)**; and (6) MMMMMRL **(SEQ ID NO: 12)**. The NAC portion was chosen because this piece of the protein has been found to aggregate in amyloid plaques in Alzheimer's disease. Particularly preferred, because of stronger binding properties, are THRLPSR **(SEQ ID NO: 5)**; SLKRLPK **(SEQ ID NO: 7)**; THIHHPS **(SEQ ID NO: 11)** and MMMMMRL **(SEQ ID NO: 12)**. Most preferred is the peptide SLKRLPK **(SEQ ID NO: 7)**.

Marked up version of the paragraph starting at page 16, lines 23-27, thru page 17, lines 1-9, is below:

α-Synuclein (wildtype, A53T and A30P) was cloned into the NotI site of pcDNA3. The sequence of each construct was confirmed by DNA sequencing. For production of recombinant protein, α-synuclein was inserted into the NcoI/NotI site of the Pro-Ex His 6 **(SEQ ID NO: 13)** vector (GIBCO/BRL). To generate recombinant α-synuclein, Bper (Pierce) reagent was used to solubilize the recombinant α-synuclein from the IPTG-induced bacterial lysates, which were then passed over a nickel-agarose affinity column, washed and eluted with imidazole according to the manufacturer's directions (GIBCO/BRL). Following purification, the His-6 tag **(SEQ ID NO: 13)** was cleaved with TEV protease and removed by passing through a nickel-agarose column. Antibodies used include: polyclonal anti α-synuclein (SC1, 1:2000 for immunoblotting and 1:500 for immunocytochemistry against human α-synuclein, residues 116-131, sequence = MPVDPDNEAYEMPSEE) **(SEQ ID NO: 14)**, monoclonal anti α-synuclein-1 (1:1000, Transduction Labs), polyclonal rabbit anti-ubiquitin (1:1000 for immunoblotting and 1:500 for immunocytochemistry, Dako).

Marked up version of the paragraph starting at page 31, lines 25-28, thru page 32, lines 1-2, is below:

Phage display (phage display kit was from New England Biolabs (Beverly, MA)) was used to specifically select for peptides that can inhibit iron binding. Phages were identified from libraries that bind to amino acids 121-131 and amino acids 61 - 87 of α-synuclein and partially inhibit iron-induced aggregation of α-synuclein. The peptides were selected using the α-synuclein 121-131 and 61-87 peptides as the bait. One such peptide has the sequence SLKRLPK **(SEQ ID NO: 7)**.

Marked up version of the paragraph starting at page 32, lines 3-12, is below:

To demonstrate that the peptide SLKRLPK **(SEQ ID NO: 7)** binds α-synuclein, the α-synuclein was absorbed to a plastic well, phage

was added at dilutions of 1: 10, 1: 100, and 1: 1000, incubated 1 hour and washed 5 times. Bound phage was detected by adding peroxidase coupled anti-phage antibody, incubating 1 hr, washing 5 times and detecting signal using the peroxidase substrate ABTS. Bound phage produces a dark green signal that is measured as optical density with a spectrophotometer. Using these conditions, the phage containing the SLKRLPK **(SEQ ID NO: 7)** peptide gave OD's of 0.882, 0.844, and 0.480 at dilutions of 1: 10, 1: 100, and 1: 1000, respectively. By contrast, another phage that did not bind gave OD's of 0.019, -0.027, and -0.554 respectively.

Marked up version of the paragraph starting at page 32, lines 18-25, is below:

The peptide has the sequence "SLKRLPK" **(SEQ ID NO: 7)**, and corresponds to a sequence expressed by a phage that shows particularly strong binding to α-synuclein by ELISA. The sequence does not contain tyrosines or tryptophans that can add to the fluorescence and complicate the analyses. This phage was generated before we understood the importance of iron for α-synuclein biochemistry (hence, the binding site was not specifically targeted against iron binding). Even so, incubating a 10- fold excess of peptide with α-synuclein reduces iron-induced α-synuclein aggregation by 38%.

In the Claims:

21. (Amended) The method of claim 20, wherein the peptide is selected from the group consisting of: WRQTRKD **(SEQ ID NO: 1)**; HYAKNPI **(SEQ ID NO: 2)**; ATINKSL **(SEQ ID NO: 3)**; RRRGMAI **(SEQ ID NO: 4)**; THRLPSR **(SEQ ID NO: 5)**; TKHGPRK **(SEQ ID NO: 6)**; SLKRLPK **(SEQ ID NO: 7)**; RLRGRNQ **(SEQ ID NO: 8)**; WPFHHHR **(SEQ ID NO: 9)**; HLYHHKT **(SEQ ID NO: 10)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

22. (Amended) The method of claim 21, wherein the peptide is selected from the group consisting of: THRLPSR **(SEQ ID NO: 5)**;

SLKRLPK **(SEQ ID NO: 7)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

23. (Amended) The method of claim 22, wherein the peptide is SLKRLPK **(SEQ ID NO: 7)**.

25. (Amended) The method of claim 24, whererin the agent is selected from the group consisting of: WRQTRKD **(SEQ ID NO: 1)**; HYAKNPI **(SEQ ID NO: 2)**; ATINKSL **(SEQ ID NO: 3)**; RRRGMAI **(SEQ ID NO: 4)**; THRLPSR **(SEQ ID NO: 5)**; TKHGPRK **(SEQ ID NO: 6)**; SLKRLPK **(SEQ ID NO: 7)**; RLRGRNQ **(SEQ ID NO: 8)**; WPFHHHR **(SEQ ID NO: 9)**; HLYHHKT **(SEQ ID NO: 10)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

26. (Amended) The method of claim 25, wherein the agent is selected from the group consisting of: THRLPSR **(SEQ ID NO: 5)**; SLKRLPK **(SEQ ID NO: 7)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

27. (Amended) The method of claim 26, wherein the peptide is SLKRLPK **(SEQ ID NO: 7)**.

35. (Amended) The composition of claim 34, wherein the peptide is selected from the group consisting of: WRQTRKD **(SEQ ID NO: 1)**; HYAKNPI **(SEQ ID NO: 2)**; ATINKSL **(SEQ ID NO: 3)**; RRRGMAI **(SEQ ID NO: 4)**; THRLPSR **(SEQ ID NO: 5)**; TKHGPRK **(SEQ ID NO: 6)**; SLKRLPK **(SEQ ID NO: 7)**; RLRGRNQ **(SEQ ID NO: 8)**; WPFHHHR **(SEQ ID NO: 9)**; HLYHHKT **(SEQ ID NO: 10)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

36. (Amended) The composition of claim 35, wherein the peptide is selected from the group consisting of: THRLPSR **(SEQ ID NO: 5)**; SLKRLPK **(SEQ ID NO: 7)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

37. (Amended) The composition of claim 36, wherein the peptide is SLKRLPK **(SEQ ID NO: 7)**.

40. (Amended) The peptide of claim 39, wherein the peptide comprises a sequence selected from the group consisting of: WRQTRKD **(SEQ ID NO: 1)**; HYAKNPI **(SEQ ID NO: 2)**; ATINKSL **(SEQ ID NO: 3)**; RRRGMAI **(SEQ ID NO: 4)**; THRLPSR **(SEQ ID NO: 5)**; TKHGPRK **(SEQ ID NO: 6)**; SLKRLPK **(SEQ ID NO: 7)**; RLRGRNQ **(SEQ ID NO: 8)**; WPFHHHR **(SEQ ID NO: 9)**; HLYHHKT **(SEQ ID NO: 10)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

41. (Amended) The peptide of claim 40, wherein the peptide comprises a sequence selected from the group consisting of: THRLPSR **(SEQ ID NO: 5)**; SLKRLPK **(SEQ ID NO: 7)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

42. (Amended) The peptide of claim 41, which comprises the sequence SLKRLPK **(SEQ ID NO: 7)**.

44. (Amended) The composition of claim 43, which comprises a peptide containing a sequence selected from the group consisting of: WRQTRKD **(SEQ ID NO: 1)**; HYAKNPI **(SEQ ID NO: 2)**; ATINKSL **(SEQ ID NO: 3)**; RRRGMAI **(SEQ ID NO: 4)**; THRLPSR **(SEQ ID NO: 5)**; TKHGPRK **(SEQ ID NO: 6)**; SLKRLPK **(SEQ ID NO: 7)**; RLRGRNQ **(SEQ ID NO: 8)**; WPFHHHR **(SEQ ID NO: 9)**; HLYHHKT **(SEQ ID NO: 10)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

45. (Amended) The composition of claim 44, which comprises a peptide containing a sequence selected from the group consisting of: THRLPSR **(SEQ ID NO: 5)**; SLKRLPK **(SEQ ID NO: 7)**; THIHHPS **(SEQ ID NO: 11)**; and MMMMMRL **(SEQ ID NO: 12)**.

46. (Amended) The composition of claim 45, which comprises a peptide containing the sequence SLKRLPK **(SEQ ID NO: 7)**.